Innovation Policies, including the US Patent System

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The material covered in these slides is partially drawn from: Bryan, Kevin and Heidi Williams (2021) "Innovation: Market Failures and Public Policies," Chapter 13 in the *Handbook of Industrial Organization Volume 4*, edited by Kate Ho, Ali Hortacsu, and Alessandro Lizzeri.

Introduction

Innovation is at the core of many fundamental economic problems

1. Technical change during the Industrial Revolution [Mokyr 2010]
2. Tradeoffs between tax-based and innovation-based climate change policies [Acemoglu et al. 2016]
3. Contribution of innovation to international agricultural development [Alston and Pardey 2014]
4. The world's seven largest private companies (as of December 2020) all produce products that had not been invented fifty years earlier

Growth potential of the modern economy is itself an innovation problem

- Are we facing a future of stagnation or is this angst merely a replay of historical worries that technological growth had come to an end? [Gordon 2017 vs. Mokyr et al. 2015]

What is innovation?

Innovation: the invention, development, and diffusion of new goods, services or production processes.

- Economic problem that depends on active choices of agents who respond to incentives
- Historically, not treated as a primarily economic concern
  - Prior to 1960, 11 articles in AER, QJE, ECTA (combined) had "invention" or "innovation" in title
  - Development and diffusion of new ideas thought to be psychological, sociological, or simply serendipitous

What about the economics of innovation?

"Economics of innovation" inspired by mid-century developments in industrial practice, government policy, and economic theory:

1. Rise of large-scale industrial research labs [Hounshell and Smith 1988]
2. Successful directed wartime science efforts
   - Led to Vannevar Bush's *Science, The Endless Frontier* [Bush 1945]
3. Schumpeter (1942): creation and diffusion of new goods was a fundamental economic problem
   - Contrast with Neoclassical welfare analysis, which holds technological frontier constant

1951 SSRC Conference: a progress report

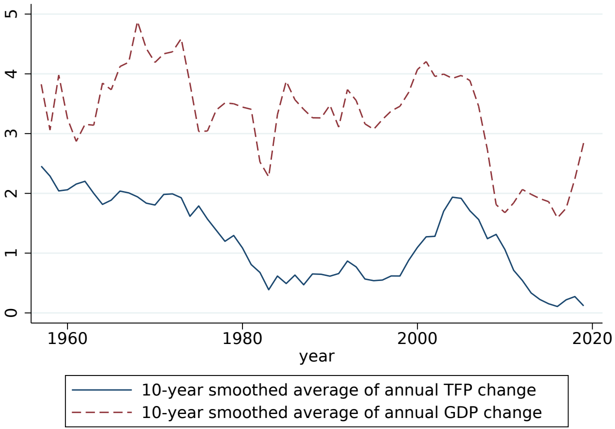
In response to newfound interest in innovation, a 1951 conference "Quantitative Description of Technological Change" was held at Princeton and supported by the Social Science Research Council

- Publication of the conference proceedings was abandoned because "the papers [were] in most cases of a very exploratory character" [Godin 2008]
- At the time, data on government R&D were close to nonexistent, very few papers had analyzed patents to study corporate innovation, and the link between these efforts and economic growth was unclear

Solow (1957): "black box" of innovation

- Share of long-run economic growth unexplained by changes in capital and labor inputs (TFP, total factor productivity) as high as 85%
- By construction, TFP is an unmeasured residual
- However, subsequent work adjusting for labor quality and capital utilization suggested much of "Solow residual" reflects technological progress

Changes in TFP and GDP over time in the US



Notes: This figure displays 10-year smoothed averages of annual changes in TFP and GDP. TFP here is the standard decomposition aside from adjusting for changes in labor and capital utilization (e.g., "labor hoarding" with shorter hours during recessions). Source: Fernald (2012).

1962 NBER Conference: a progress report

Core questions of innovation research agenda:

- How do inventors choose the rate and direction of the research investments they pursue?
- What market structure leads to high levels of innovation?
- Is innovation optimally generated with laissez faire incentives?

Raised in groundbreaking 1962 in NBER conference volume on the Rate and Direction of Inventive Activity and related papers published by the economists who attended the event [NBER 1962, Machlup 1962, Nelson 1959, Schmookler 1962 and 1966]

Despite 60 years of extensive research since the 1962 conference, these questions remain largely open.

Summary of the core problems

1. What market failures exist in the production and diffusion of new goods? [Arrow 1962; quantifying social and private returns to innovation as in Jones-Summers 2021, Bloom et al. 2013]
2. How does inefficiency in the production of innovation harm growth? [Ben's lecture]
3. What makes empirically analyzing innovation policy questions challenging, and how have economists made progress in measurement and empirical analysis? [today + my second lecture]

Outline

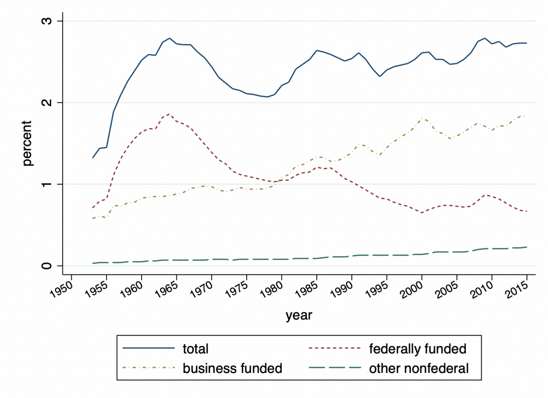
Background

One of the most important ways in which the public sector supports innovation is through the direct funding of research

Federally funded R&D used to be the primary component of total US R&D spending, but that since about 1980 the private sector has grown to account for a higher share of US R&D spending

- This federal research support involved fifteen federal government departments and a dozen other agencies
- By far the largest two supporters were the Department of Defense (DOD) and the Department of Health and Human Services (HHS, which includes the National Institutes of Health or NIH)

US research and development as a share of GDP, by source of funds: 1953-2015



Notes: This figure shows US research and development (R&D) spending – total and by source – as a share of GDP from 1953 to 2015. Source: Appendix Table 4-1 of National Science Foundation (2018).

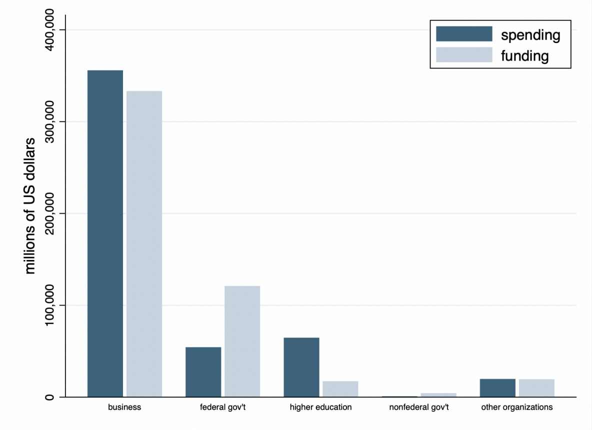
Use of federal funding

Federal funding consists of two distinct activities:

- Conducting research directly (e.g. federally funded research and development centers (FFRDCs) such as Los Alamos National Laboratory)
- Supporting external research (e.g. NIH grants to university researchers)

The following figure illustrates an important pair of asymmetries: the federal government funds more external research than it spends internally, whereas higher educational institutions spend more than they directly fund

Spending on and funding of US R&D by sector: 2008-2015



Notes: This figure shows spending on and funding of US R&D by sector from 2008 to 2015.
Source: Table 4-1 of National Science Foundation (2018)

Value of public research support

On the social value of federal funding: How different is the set of innovations society has access to because of public research support?

- Available evidence from qualitative case studies suggests that many or most scientific discoveries can trace their roots to both public research support and investment by private firms
- For example, Chakravarthy, Cotter, DiMasi, Milne, and Wendel (2016) traces the history of 19 transformative drugs in the past 25 years, and finds only 4 have been researched and developed solely by one sector

Returns to public research funding

Central policy question: what is the return to incremental dollars of public research funding?

- For example, consider the "war on cancer"
  - 1971 – Pres. Nixon introduces National Cancer Act, which gives National Cancer Institute special authority to spend (flexibly) on priorities related to cancer
  - Additional $100 million for cancer research
- Many have declared the War on Cancer a failure
- Rigorously analyzing success/failure is challenging

Challenge #1: finding a paper trail

We often lack a paper trail for measuring the impacts of research investments

- For example - if the war on cancer funded investments into cell signaling that formed the basis for the development of a leukemia treatment, what data would allow us to trace that connection?

Researchers have made progress on this measurement challenge; here, we'll focus on Sampat and Lichtenberg (2011) to illustrate this point

Sampat and Lichtenberg (2011)

Sampat and Lichtenberg (2011) developed direct and indirect measures of whether drugs approved by the US Food and Drug Administration (FDA) built on publicly supported research

- Direct support: whether patents linked to the individual FDA-approved drugs are assigned to government agencies and whether they disclose a so-called government interest statement
- Indirect support: whether drug patents cite earlier patents assigned to government agencies or patents disclosing government interest statements, or cite published biomedical research articles that acknowledge public research support

Authors estimate while only 9% of new drugs approved by the FDA between 1988-2005 directly benefited from public research support, nearly half (47.8%) benefited indirectly

Challenge #2: Constructing a control group

Building appropriate control groups is important, but difficult, for measuring the impact of public research

- Public research funding often targets areas that are scientifically promising
- Shifts over time in the scientific potential of a given area would be expected to affect incentives for both private and public research investments
- If a dollar of public research crowds out a dollar of private research, then public research could in theory have no real effect on total research spending [David et al. 2000]

Jacob and Lefgren (2011)

Key advances have been made in the context of understanding NIH support for biomedical research

- Jacob and Lefgren (2011) make advances in constructing “treatment” and “control” groups in the context of NIH support for biomedical research
- Applications are assigned priority scores based on independent scientific reviews
- Grant applications just above and just below the priority score cutoff should be similar ex ante, but differ ex post in their probability of receiving funding
- Using an RD design, the authors estimate that receiving an R01 grant (roughly $1.7 million) leads to one additional publication (7% increase) over the next 5 years

Azoulay, Graff Zivin, Li, and Sampat (2019)

Builds on the data from Sampat and Lichtenberg (2011) and the empirical approach of Jacob and Lefgren (2011) to estimate the impact of NIH funding on private-sector patenting

- The NIH comprises 21 institutes/centers, each receiving congressional appropriations
- Applications are assigned raw scores which are normalized to ranks
- Institutes/centers make funding decisions with a rank cutoff
- With an RD approach similar to Jacob and Lefgren, and a linkage between grants, papers, and citing patents, the authors estimate that $10 million in NIH funding leads to 2.7 additional patents

Areas for future work: going beyond the NIH

Much of the progress on measurement and empirical approaches for estimating return to public research spending focused on NIH data

- More work can be done to analyze the impacts of research funding from other federal departments and agencies
- Moretti, Steinwender, and Van Reenen (2019) analyzes how defense-related research spending affects private research spending
- Gross and Sampat (2020) uses World War II scientific funding to examine long-run shifts in the rate, direction, and location of US technological development

Future work: funding structure

Federal funding is often structured in different ways, which could vary in effectiveness

- Some research grants like NIH R01 grants provide 3-5 years of funding to support specific projects
- In contrast, programs like the Howard Hughes Medical Institute (HHMI) Investigator Program fund researchers, who have more project flexibility, over a longer time period
- Theoretical work (e.g. Manso (2011)) finds differing incentives, backed by empirical evidence from Azoulay, Graff Zivin, and Manso (2011)
    - R01-style contracts may motivate incremental refinements on past discoveries
    - HHMI-style contracts provide researchers with more freedom to pursue radical and untested ideas

Future work: rethinking peer review

Funding programs often have different methods for deciding which applications receive grants

- Institutions such as the NIH rely heavily on peer review by field-specific experts
- Li (2017) finds that evaluators are both better informed and more biased about the quality of projects closer to their own work
- Li and Agha (2015) finds that higher peer-review scores are associated with better research outcomes

Are there better ways of selecting which grant applications receive funding?

Future work: alternatives to peer review

Criticisms of peer review:

- Disadvantages early career scholars and scholars from diverse backgrounds
- Poorly evaluates the work of multidisciplinary teams
- Imposes large costs on both applicants and reviewers

Alternative allocation mechanisms:

- Randomization for borderline grant decisions could reduce evaluator bias (currently used by the New Zealand Health Research Council)
- Methods that cut down on evaluation delays and grant preparation time could also improve project quality

Future work: developing innovation from universities

Considerable academic and policy interest in how best to encourage the development of innovations out of universities, particularly following the 1980 Bayh-Dole Act

- The Bayh-Dole Act allowed federal grantees like universities to obtain patents on inventions created by their funded research
- Lach and Schankerman (2008) finds that raising researchers' royalty shares increases university licensing income
- Ouellette and Tutt (2020) argues this result is driven by errors in the coding of university policies, and that there is no evidence that royalties impact licensing outcomes at US universities
- Other work in this area has focused on university innovation in European contexts (e.g. Hvide and Jones (2018))

Future work: investments in scientific infrastructure

- In addition to funding research applications or scientific education, governments also fund large, shared infrastructure such as the early internet, particle colliders, and biological repositories
- However, measuring the relative efficiency of infrastructure investments versus direct funding in the aggregate is challenging
- In the long-run, physical capital appears more replaceable than human capital
  - Waldinger (2016): no long-run relationship between physical destruction during World War II and scientific output
  - Dismissal of elite scientists from their posts before the war led to permanent declines in science in a given city

Outline

Market-based innovation policies

- From Schmookler (1966): "invention is largely an economic activity which, like other economic activities, is pursued for gain"
- Intuition and empirical evidence tell us that changing costs and rewards facing firms can change research investments

Examples of research incentives

Economic theory and the available data support the idea that incentives should drive research investments. If most scientific advances were to happen via lucky accidents, economics – and policy – would have little role to play.

Example: As the US population has aged, investments in drug development have shifted towards developing more drugs to treat diseases common in older age groups [Acemoglu and Linn 2004]

Designing economic policy

The government has two levers for shifting the rate and direction of inventive activity:

- Reduce costs with tax credits, direct subsidies, or labor market policies such as immigration changes that make it easier for firms to hire specialized workers
- Increase expected revenues by changing antitrust policy or awarding market power or payoffs directly via the patent system or prizes

Specific areas of innovation policy: taxes, intellectual property (IP), competition, and labor market. Focus today on IP / patents.

Outline

Intellectual property rights (IPR)

Formal intellectual property (IP): *a set of government policies which grants special rights to exclude others from producing, selling, licensing, or building on products, resulting in less competition than would be faced in a free market*

Unlike taxes and subsidies, IP affects both the cost of research and the reward to research:

- Cost: can require inventors to license ideas they wish to build on
- Reward: limits ex-post competition

This lecture focuses on one form of IP: patents

The patent application process

This lecture focuses on the U.S. Patent and Trademark Office (USPTO), but discusses various dimensions of international patenting

- When filing a new patent application, inventors must submit a written description of their invention
  - Includes a discussion of "prior art": publicly available information relevant to the originality of the patented invention
  - Includes a specific list of claims that the applicant seeks to assert intellectual property rights over
- Applicants pay filing fees varying by type of application and applicants' entity size
  - Cost of filing a patent: $10,000 to $40,000
    - ★ Serves as a barrier to startups and other small firms [Graham 2009]

Patent review process

1. After submission, patent application is assigned to a group of patent examiners with relevant technological expertise, and assigned to a specific examiner for review
   - Examiners determine whether the application meets the standard for patentability
     - Claimed inventions: must be patent-eligible, novel, non-obvious, and useful
     - Text of patent: must meet requirements for disclosure and claim definiteness

2. Examiners can either issue a first action allowance (i.e. grant the patent) or issue a de facto rejection, allowing applicants the opportunity to revise their submission
   - The patent application review process often involves multiple rounds of rejection and revision
   - Patent applications cannot be rejected by the USPTO, only abandoned by applicants [Lemley and Sampat 2008]

How many patents does the USPTO grant?

Patent reform debates often focus on whether the USPTO grants "too many" or "too few" patents

This debate has a long history:

- Machlup and Penrose (1950) discuss the 19th century patent abolition movement
- Polanvyi (1944) presents conceptual arguments against patents in the context of industrial research
- More recently, debates have considered whether the USPTO's bar for novelty might be too low – resulting in too many new grants

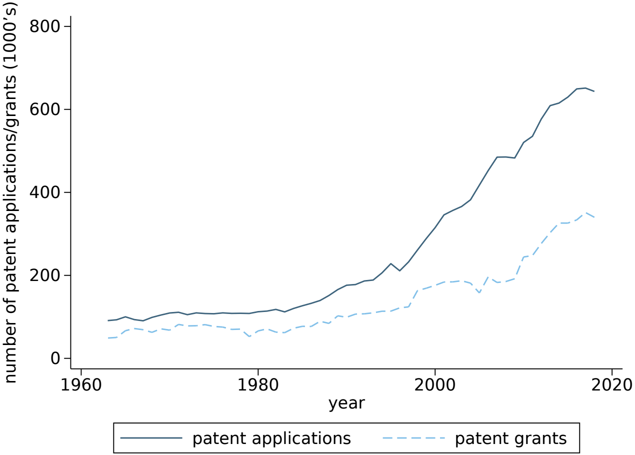
Before attempting to answer whether the grant rate is too high/low, we first consider the challenge of measuring the USPTO's grant rate

Challenges finding the patent grant rate

- Data on patent applications and grants are made publicly available
  - Historically, records of successful applications and their associated grants were available
  - Until recently, unsuccessful applications were not reported, complicating measurement efforts
- Even when unsuccessful applications can be observed, it is not clear how long after an initial submission a final allowance or rejection will occur
  - Rounds of rejection and revision can unfold quickly or slowly depending on the USPTO's review lags and applicants' timeliness in resubmitting
- Closely related patent applications – including continuations and divisionals – may be produced at some point during the prosecution process and can contain ideas from the original grant
  - How should these be incorporated?

The following figure tabulates counts of USPTO applications and grants by year from 1963-2019

USPTO patent applications and grants by year, 1963-2019



Notes: These totals include utility, design, and plant patents as well as patent reissues. Source: USPTO Patent Technology Monitoring Team (2021)

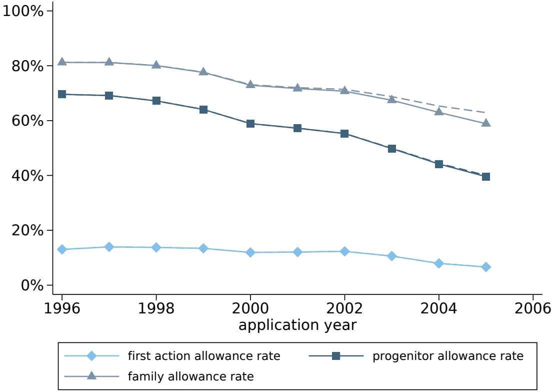
Measuring grant rates

- Carley, Hedge, and Marco (2015) uses non-publicly available USPTO administrative data including *all* applications
- Analysis identifies "progenitor" patents (patent applications not derived from previous applications)
- Authors also look at a "family allowance rate," incorporating patent grants that accrue to continuations or divisionals derived from the original application

Findings suggest that initial (first action) allowances are relatively infrequent, but that progenitor allowance rates are much higher

- Suggests that many applications are granted patents only after at least one revision

USPTO allowance rates for applications filed from 1996-2005 and examined before mid-2013



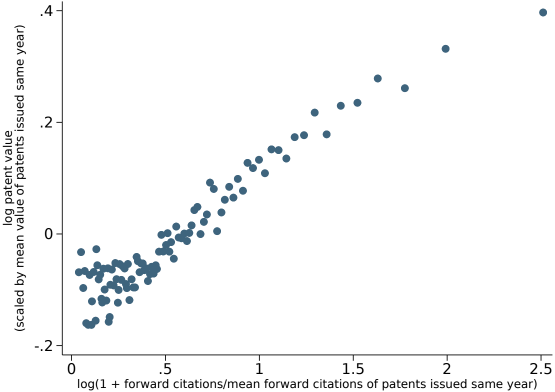
Note: The dashed lines represent the highest possible allowance rates (i.e., the allowance rate assuming that every pending application as of June 30, 2013 is allowed). Source: These totals include utility, design, and plant patents as well as patent reissues. Source: Carley, Hedge, and Marco (2015)

Value of patents

The value distribution of granted patents is quite skewed, so patent counts can be misleading [Pakes 1986]

- How to measure the value of granted patents?
  - Forward patent citations [Trajtenberg 1990]
  - Patent renewals [Bessen 2008, Pakes 1986, Schankerman and Pakes 1986]
  - Licensing revenue [Abrams et al. 2019]
  - Excess stock market returns [Kogan et al. 2017]
- These metrics capture different quantities: excess stock market returns measures the "surprise" component of private returns to a patent at the time of grant, and forward citations aim to capture spillovers
  - Nevertheless, these measures have a strong, positive correlation

Forward citations and market value (1926-2010)



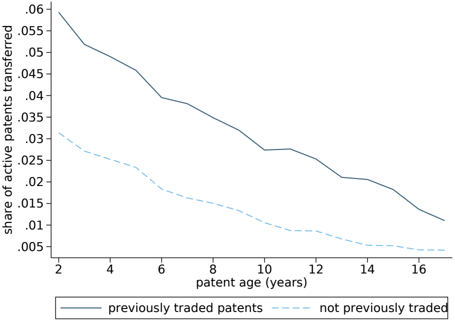
Note: This figure plots the cross-sectional relationship between forward patent citations and the estimated excess stock return patent value estimate constructed by Kogan, Papanikolaou, Seru, and Stoffman (2017), which is defined only for granted US patents assigned and linked to publicly traded firms. Sources: Kogan, Papanikolaou, Seru, and Stoffman (2017) and USPTO administrative records

Other patent basics

- USPTO-granted patent rights don't extend to foreign markets, so inventors wanting IP rights abroad must file a separate application in that region
- Granted patents require maintenance fees to remain active
- If patents are active, owners can enforce patent rights with litigation
  - Only 1-2% of patents are litigated, though others are challenged and settle out of court
  - Valuable patents are more often targets of legal action
- Patents can change ownership and owners may record these changes with the USPTO
  - See Serrano (2010) for an examination of recorded ownership changes

Share of active patents traded (conditional on any previous trading)

Previously traded patents are more likely to be traded again, and probability of ownership changes declines with patent age [Serrano 2010]



Note: This figure is similar to Serrano (2010). Source: Marco, Myers, Graham, D'Agostino, and Apple (2015)

Proliferation of patent data

- Digital full-text versions of patent grants since 1976 are publicly available
- Each step of the application process is now publicly documented in the Patent Application Information Retrieval (PAIR) data
  - Enables modern text analysis methods to compute text-based measures of patent quality
  - Allows extraction of data on citations, inventor locations, assignees, claims, and more

Outline

Empirical evidence on patents

Patents are traditionally seen as trading off the benefit of more invention against the cost of higher prices during the life of the patent

- The more effective patent laws are at encouraging research investments, the stronger the case for stronger IP rights
- Historical literature: market incentives help encourage innovation, and patents help facilitate the market for technologies [Khan and Sokoloff 1993, Lamoreaux and Sokoloff 1999, Lamoreaux et al. 2013]

However, several papers failed to uncover evidence that stronger patents induce more R&D [Lerner 2009, Moser 2005, Sakakibara and Branstetter 2001]

Patents by industry

Industries that stand out as exceptions to the nonimportance of patents:

- Pharmaceuticals
  - Surveys and data are consistent with patents having an economically important effect on R&D [Cohen et al. 2000, Levin et al. 1987, Mansfield 1986, Budish et al. 2015]
- Agriculture
  - The introduction of patent protection for plant biotechnology in the late 1980s increased the development of novel plant varieties
  - Further, US counties more exposed to the policy change saw agricultural land values and profits increase [Moscona 2020]
- Chemicals
  - Evidence from surveys shows relatively heavy patent use for chemicals, including for blocking rivals [Cohen et al. 2000, Levin et al. 1987, Mansfield 1986]

Stunting follow-on innovation

Intellectual property rights in the form of patents or copyright-type agreements can hinder follow-on innovation [Galasso and Schankerman 2015, Williams 2013]

- These results are collectively in line with Green and Scotchmer (1995)
- Patents are more likely to be harmful when the precise follow-on inventions they cover are unclear, or when follow-on inventors are worried about holdup from "submarine patents"
- The assumption that patents hinder follow-on innovation has informed a recent set of important US Supreme Court decisions restricting the set of discoveries eligible for patents

Measuring patenting and innovation

Finding appropriate data to analyze the effects of patent policy has been challenging

- While researchers frequently use patents to measure innovation, changes in patent law can affect costs and benefits of filing for patent protection
- Since these costs/benefits affect the propensity to patent, changes in patenting and changes in innovation are often conflated
- Example: Abrams (2009) studies patent term extensions from TRIPS
  - Abrams tests whether technology classes with longer patent term extensions saw increases in patent counts
  - Hard to interpret results since the policy change altered incentives to file for patents on existing research investments

Measuring patenting and innovation

Two clever solutions to this concern

Lerner (2009)

- Analyzes changes in patenting behavior of inventors both in a country experiencing a patent law change *and in foreign markets* where no such measurement challenge arises
- Finds little response of innovation to strengthened patent laws

Galasso and Schankerman (2015)

- Analyses how follow-on innovation (as measured by patent citations) change when a focal patent is invalidated
- Finds that citations to invalidated patents rise substantially following invalidation, suggesting patent-related frictions which harm sequential innovation

Using real-world outcomes

Another way to accurately measure how innovation changes in response to patent policy: link patents with real-world outcomes

- Moser, Ohmstedt, and Rhode (2018) use the yields of plants covered by plant patents
- Murray and Stern (2007) use citations to scientific papers disclosing the same knowledge as a given set of patents
- Sampat and Williams (2019) link patents with the genes they claim as intellectual property

Empirical variation

- Economists also need sources of empirical variation to analyze the effects of IP rights
- This is challenging due to the uniform protection provided by the patent system across technologies and countries

Some historical cross-country variation is useful:

- Many papers test how country-level patent protection affects country-specific drug launch decisions [Cockburn et al. 2016, Duggan et al. 2016, Kyle and Qian 2014]
- Moser (2005) tests how country-specific patent laws affect the direction of technology change within a country

Still, inventions are often developed for a global market, and patent law changes in "small" countries likely have little effect on global incentives for innovation

New empirical strategies

Recent empirical tests on the effects of IP rights have leveraged administrative data

- Galasso and Schankerman (2015) leverages the quasi-random assignment of judges to cases at the US Count of Appeals for the Federal Circuit to study patent invalidation effects
- Sampat and Williams (2019) leverages the quasi-random assignment of patent applications to patent examiners at the USPTO to study patent grant effects
  - The Sampat-Williams approach has been further improved by Feng and Jaravel (2020) and Righi and Simcoe (2019)

Areas for future work

- Patent scope [Sakakibara and Branstetter 2001, Lerner 1994]
- Costs and benefits of the disclosure function in the patent system [Ouellette 2012, Roin 2005]
- Alternatives to patents for encouraging innovation [e.g. Anton and Yao 1994, Gallini and Scotchmer 2002]
  - e.g. prizes, contests, patent buyouts, and laissez faire alternatives such as secrecy and first-mover advantage
- The role of excludability and open access [e.g. Bryan and Ozcan *forthcoming*, Williams 2013]

Why having empirical evidence matters

- Should we have stronger or weaker patent regimes?
  - For pharmaceuticals: key role for FDA exclusivity periods

- In the absence of better evidence, the assumption that patents hinder follow-on innovation has informed recent US Supreme Court decisions restricting the set of discoveries eligible for patents
  - *Bilski v. Kappos*: patents on abstract ideas (investment strategies)
  - *Mayo v. Prometheus*: patents on laws of nature (diagnostic methods)
  - *AMP v. Myriad*: patents on natural phenomena (human DNA)
  - *Alice Corp v. CLS Bank*: patents on abstract ideas (software)

Outline

1. Introduction to innovation policies
   - Funding scientific research
   - Market-based innovation policies

2. Introduction to the US patent system
   - A primer on patents
   - Intellectual property: evidence
   - Research papers as progress reports
     - Example #1: Budish et al. (2015)
     - Example #2: Sampat-Williams (2019)
   - Intellectual property: theory

Are we getting the right medical technologies developed?

American Economic Review 2015, 105(7): 2044–2085
http://dx.doi.org/10.1257/aer.20131176

Do Firms Underinvest in Long-Term Research? Evidence from Cancer Clinical Trials†

By Eric Budish, Benjamin N. Roin, and Heidi Williams*

Motivation

- Over last five years, eight new drugs approved to treat lung cancer
- All eight were approved based on evidence of incremental survival improvements in patients with most advanced form of the disease
  - Well-known example: Genentech's Avastin (10.3 vs. 12.3 months)
- In contrast, no drug has ever been approved to prevent lung cancer, and only six drugs have ever been approved to prevent *any* cancer

This paper

- While this pattern could solely reflect market demand or scientific challenges, in this paper we investigate an alternative hypothesis: private firms may (differentially) underinvest in long-term research
  - Late-stage cancer drugs can be brought to market comparatively quickly, relative to early-stage treatments or preventatives
    - Key: Time required to show a statistically significant treatment effect
  - Excess impatience or patents may under-incentivize long-term research
- We document that such underinvestment is quantitatively significant in markets for cancer drugs, and analyze potential policy responses

Two examples: Prostate cancer drugs

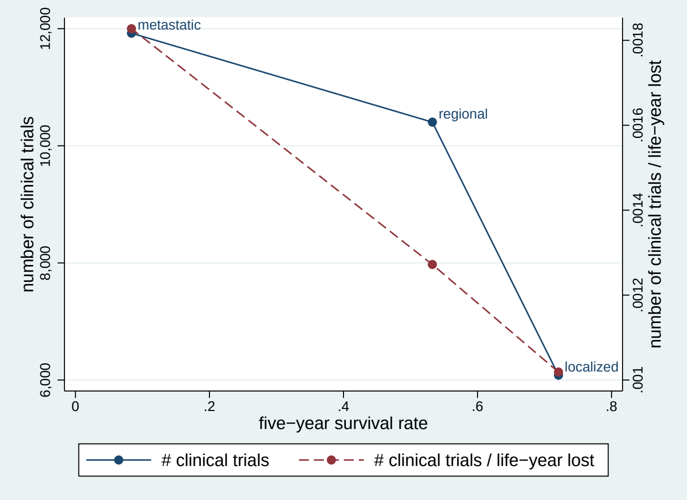
1. de Bono *et al.*: Metastatic patients (5-yr survival $\approx$ 20%)
   - Median follow-up time for measuring patient survival: 12.8 months
   - Trial length: 3 years
2. Jones *et al.*: Localized patients (5-yr survival $\approx$ 80%)
   - Median follow-up time for measuring patient survival: 9.1 years
   - Trial length: 18 years

Consistent with commercialization lags distorting private R&D incentives:

- Metastatic clinical trial funded by Cougar Biotechnology
- Localized clinical trial funded by US National Cancer Institute

We construct data on all such clinical trials over the last three decades, which we match to data on patient survival over the same period

Survival time and R&D investments: Stage-level data



Notes: See Figure 1(a) in paper.

How to interpret this fact?

By itself, this fact is difficult to interpret for two reasons:

1. Correlation need not reflect a causal relationship between commercialization lags and R&D investments
2. Even if this correlation did reflect a causal relationship, it need not be evidence of a distortion because the social planner is also more likely to pursue research projects that can be completed more quickly

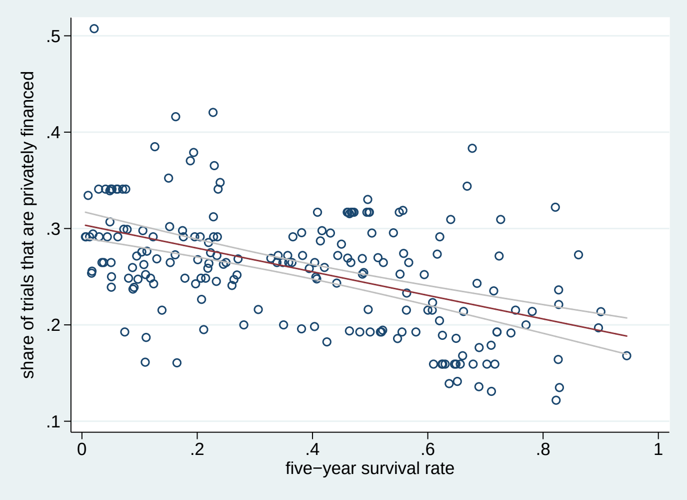
Surrogate endpoints and R&D investments

This suggests that there is a causal relationship: if commercialization lags were shortened, there are scientific opportunities available that would be pursued.

Notes: See Figure 4 in paper.

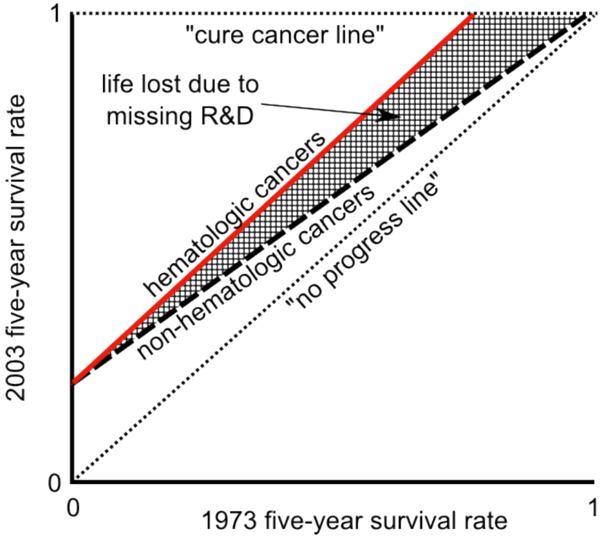
Share of clinical trials that are privately financed

Taken together, this - together with the surrogate endpoints evidence - provides support for the idea that commercialization lags distort private R&D investments.



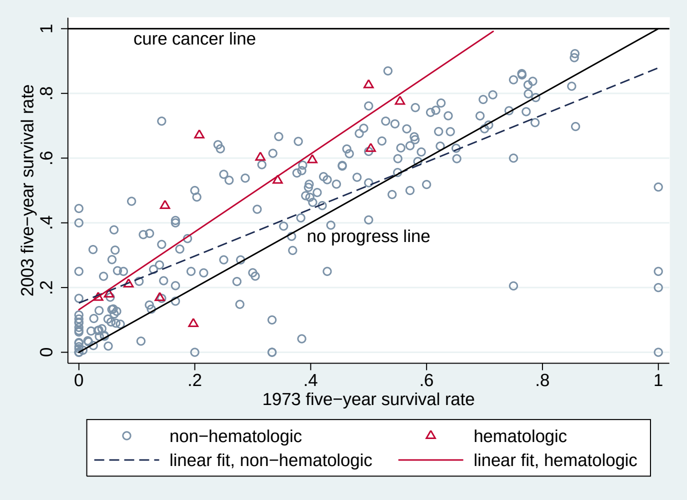
Notes: See Figure 5(b) in paper.

Counterfactual: Survival gains, 1973-2003



Notes: See Figure 6(a) in paper.

Counterfactual: Survival gains, 1973-2003



Notes: See Figure 6(b) in paper.

Rough back-of-the-envelope: Value of lost life

Value of life lost among US cancer patients diagnosed in 2003:

1. Using the cancer registry data, we translate the gap between the hematologic and non-hematologic survival curves into an estimate of life-years lost per cancer patient: 1.07 life-years per patient
2. For each cancer-stage, multiply by the number of US patients$_{cs}$ diagnosed in 2003: 890,000 life-years lost for that cohort
3. Multiplying by a standard value of a statistical life-year (Cutler 2004: \$100,000) monetizes this lost life at a value of \$89 billion

Take-aways

- Our evidence is directly relevant to two policy levers:
  1. Allowing firms to rely on valid surrogate endpoints
  2. R&D subsidies targeting long commercialization lag projects
- Estimates cannot speak directly to patents

Anecdote: Surrogate endpoints and heart disease

- Heart disease is the leading cause of death in the US, but the age-adjusted rate of death has dropped by 50% since 1968
- Decline largely attributed to beta-blockers, ACE-inhibitors, statins
- These drugs were approved based on blood pressure, LDL cholesterol
  - Surrogates first identified by decades-long Framingham Heart Study
  - Some have argued that w/o surrogate endpoints, these drugs may not have reached the market [Lathia et al. (2009); Meyskens et al. (2011)]

Both our empirical evidence for cancer and this historical case study for heart disease suggest that research investments aimed at establishing and validating surrogate endpoints may have a large social return

Outline

Should human genes be patentable?

Intellectual Property Rights and Innovation: Evidence from the Human Genome

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https://doi.org/10.1257/aer.20151398

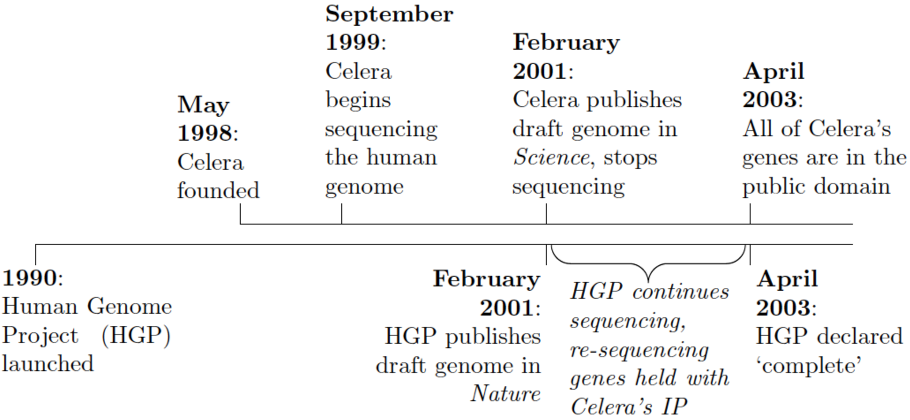
How Do Patents Affect Follow-On Innovation? Evidence from the Human Genome†

By Bhaven Sampat and Heidi L. Williams*

To fix ideas

- Suppose the firm Celera holds IP on a human gene
- Suppose Pfizer discovers a diagnostic test based on Celera's gene
- Will Celera's IP discourage Pfizer from developing this test?
    - In a perfect contracting environment, Celera and Pfizer would negotiate a license such that cumulative research is not hindered
    - However, transaction costs - *e.g.* private information about R&D costs - may cause licensing negotiations to break down

Empirical context: Sequencing of the human genome

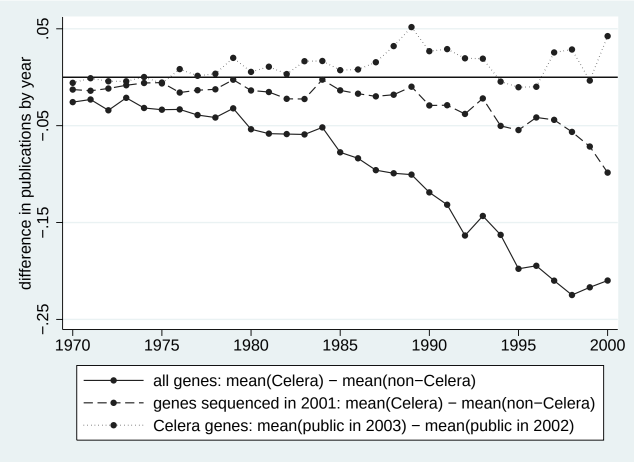


Notes: See Figure 1 in paper.

Data: An example

- RAX2 gene (*NM_032753.3*)
- RefSeq: appears in 2001
  - Istrail *et al.* (2004): never held with Celera's IP
- OMIM: RAX2 studied in *Human Molecular Genetics* (2004)
- OMIM: two RAX2 genotype-phenotype entries
  - Age-related macular degeneration (ARMD)
  - Cone-rod dystrophy
- GeneTests.org: ARMD test available (as of 2009)

Investigating selection into Celera's IP



Notes: See Figure 3 in paper.

No evidence of selection in Celera sample

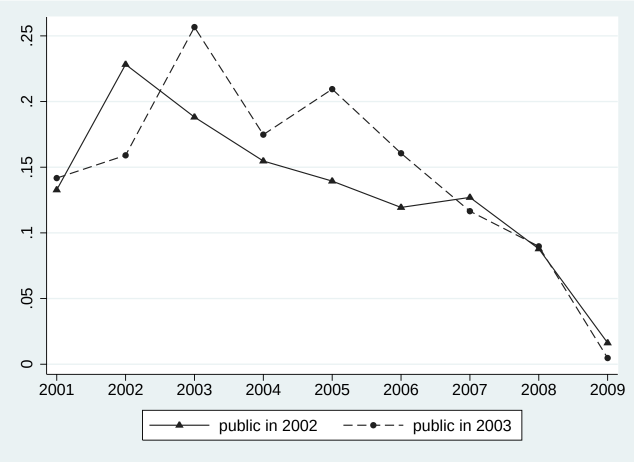
Innovation outcomes for Celera and non-Celera genes sequenced in 2001

	(1) Celera mean	(2) Non-Celera mean	(3) difference [(1)-(2)]	(4) *p*-value of difference
publications in 2001-2009	1.239	2.116	-0.877	[0.000]
1(known, uncertain phenotype)	0.401	0.563	-0.162	[0.000]
1(known, certain phenotype)	0.046	0.073	-0.027	[0.000]
1(used in any diagnostic test)	0.030	0.054	-0.023	[0.000]
N	1,682	2,851		

Notes: See Table 1 in paper.

Taken at face value: Celera's IP led to economically and statistically significant reductions in subsequent R&D, on the order of 20-30 percent

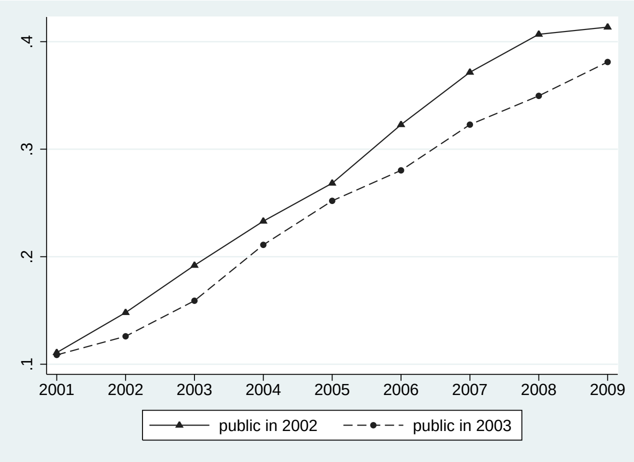
Celera genes: Publications



Notes: See Figure 5(a) in paper.

Flow of scientific effort into these two cohorts converged over time

Celera genes: 1(known, uncertain phenotype)



Notes: See Figure 5(b) in paper.

Stock of scientific knowledge is persistently lower for 2003 cohort

US Supreme Court: *AMP v. Myriad*

US Supreme Court decision (June 2013) asserted that DNA patents *"would 'tie up'...such tools and...inhibit future innovation..."*

- My estimates were cited in several briefs filed in the case
- Concern: my paper didn't analyze gene patents!

2013 *Science* article by Eliot Marshall:

Lock Up the Genome, Lock Down Research?

Researchers say that gene patents impede data sharing and innovation; patent lawyers say there's no evidence for this

Do these results apply to gene patents?

Address two key challenges that have hindered past research:

1. Measurement: Which genes are patented? [Jensen-Murray 2005]
2. Inference: How can we construct an appropriate counterfactual?
   - Using administrative data on successful and unsuccessful USPTO patent applications, we construct two new quasi-experimental methods:
     1. Compare accepted and rejected applications
     2. Use the "leniency" of the — conditionally randomly assigned — patent examiner as an instrument for which applications are granted patents [Cockburn et al 2003; Lemley-Sampat 2012; Kling 2006 and others]
   - Note: Both sources of variation useful in other applications

Example: US patent application 08/483,554

US005747282A

United States Patent [19]
Skolnick et al.

[11] **Patent Number:** **5,747,282**
[45] **Date of Patent:** **May 5, 1998**

[54] **17Q-LINKED BREAST AND OVARIAN CANCER SUSCEPTIBILITY GENE**

[75] Inventors: **Mark H. Skolnick**; **David E. Goldgar**; **Yoshio Miki**; **Jeff Swenson**; **Alexander Kamb**; **Keith D. Harshman**; **Donna M. Shattuck-Eidens**; **Sean V. Tavtigian**, all of Salt Lake City, Utah; **Roger W. Wiseman**; **P. Andrew Futreal**, both of Durham, N.C.

[73] Assignees: **Myraid Genetics, Inc.**; **University of Utah Research Foundation**, both of Salt Lake City, Utah; **The United States of America as represented by the Secretary of Health and Human Services**, Washington, D.C.

[21] Appl. No.: **483,554**

[22] Filed: **Jun. 7, 1995**

What is claimed is:

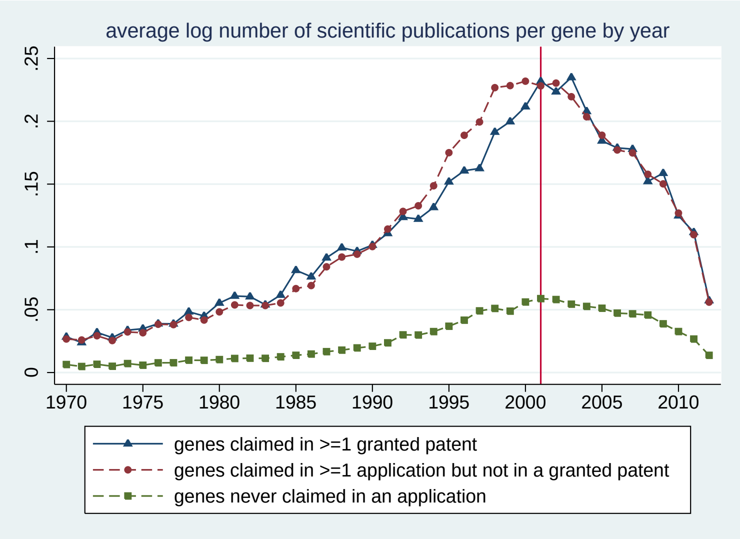
1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:1:

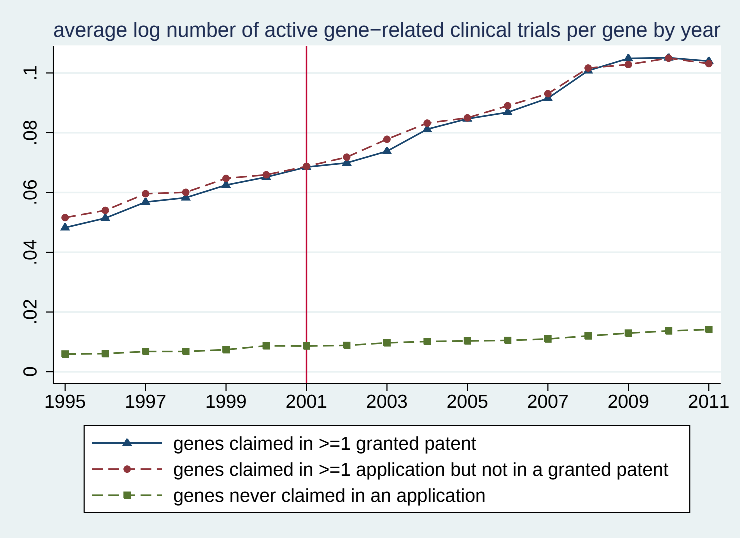
ATG GAT TTA TCT GCT CTT CGC GTT GAA GAA GTA CAA AAT GTC ATT AAT

Follow-on scientific research: Publications



Notes: See Figure 2(b).

Follow-on scientific research: Clinical trials



Notes: See Figure 2(c).

Take-aways

- Section 101 debate often framed as patents vs. public domain
  - But in the absence of patents, firms can often rely on other intellectual property, which – at least here – look worse for society than patents
- Section 101 debate also often ignores potential benefits of entry
  - Relevant question in this context: did Celera's entry result in society having access to the sequenced human genome more quickly?

- I don't (yet) have answers to all of these questions
- However, I suspect that in many contexts these factors push in opposite directions, and generate a real trade-off that requires empirical evidence on the magnitudes of multiple factors

Take-aways from a different perspective

1. Research papers as progress reports
   - Internal vs. external incentives for timing of disclosure
2. Research in teams
3. Publishing null results
4. The discomfort of referees asking you to change your question

Outline

Patent rights

Patents take a nonrival resource – knowledge – and create artificial scarcity

- Idea of patents dates back to 15th century Venice [Comino et al. 2020]
- At odds with traditional notions of property rights, in which property rights *address* the problem of scarcity

Theoretical rationale for patents is essential in understanding their use as a policy lever

Theoretical benefits of patents

Four main benefits of patents:

1. Allow inventors to appropriate more of the social value of their invention
2. Reward inventors for their contribution to future inventions enabled by their idea
3. Allow licensing markets
4. Force secrets related to the invention to be disclosed

Theoretical costs of patents

Four main costs of patents:

1. Patent holders can charge above marginal cost
2. Limit diffusion if there are transaction costs
3. Cause excess spending on races to acquire patents or attempts to "invent around" the patent ex-post
4. Sometimes distort the direction of innovation

Early arguments for patents

- John Bates Clark: "If an invention became public property the moment that it was made, there would be small profit accruing to any one from the use of it and smaller ones from making it" [Clark 1915]
- Jeremy Bentham: Patents ensure the net social value of an invention exceeds the net private value if the cost of the invention cannot be recouped before competition arrives [Bentham 1825]
  - Patents allow inventors to "sow what they reap"
  - Downside: inventions conceived as a byproduct of normal production or as a result of luck or curiosity do not require patent protection

Ex-ante competition: patent races

Ex-ante competition plays an important role in shaping research incentives

- Patent race model of Loury (1979): patent arrival rate is a function of each firm's research effort, set prior to the game as a fixed cost
  - Firms overinvest in R&D because they do not account for the fact that their effort lowers the probability rival firms will invest
- Lee and Wilde (1980) alters the Loury model, allowing firms to only pay for R&D while they are researching
  - Firms still put too much effort into R&D
- Reinganum (1982) and Judd (2003) extend patent races to differential games where firms can choose research intensity over time and value of inventions vary

Sequential innovation problem

Patents also protect inventions which build on initial inventions

Green and Scotchmer (1995): with sequential invention, not enough total social value to provide effective incentives on the margin for each investor

- Firm A can invent a product (cost c_1) with no social value, but it makes a second invention possible
- Firm B can develop follow-on invention (cost c_2) with social value v
- Optimal to invent both products if $v > c_1 + c_2$, but marginal value of *each* invention is v
- Say c_1 is close to zero, c_2 nearly equals v
- Firm A won't invest if its patent doesn't cover follow-on invention, and otherwise Firm B may not invest due to licensing negotiations

More on sequential innovation

From Green and Scotchmer (1995): optimal sequential invention depends on a) patents covering follow-on inventions for early inventors, and b) identification of future inventors before they sink R&D costs

- Denicolo (2000) counters that strong patent rights for initial inventors create even more patent races
- Gallini (1992): if it is possible to invent substitutes for a patented invention at cost, then long-lived patents can cause more competition in the short-run by inspiring the invention of these competing products

In sum, patents theoretically affect ex-ante incentives to perform R&D, ex-post sequential invention, and the type of invention firms pursue

Potential effects of sequential innovation

The sequential nature of innovation, where IP affects incentives to invent directly today and by changing the nature of competition tomorrow, can lead to some counterintuitive results

- Acemoglu and Akcigit (2012): firms who invent with large technological leads should get stronger patents
  - incentivizes leaders to keep working
  - incentivizes laggards to prevent large leads from developing
- Static models with one-shot inventions may miss incentive effects from endogenous dynamic market structure

Patent tradeoff is deeper than simply balancing monopoly distortions against the provision of quasirents to incentivize costly research

Role of 'the planner'

If the planner knows the social value and expected R&D cost of an invention, then they can pay the lowest-cost inventor their expenses and induce all inventions with net positive social value [Wright 1983]

But will planners pay inventors ex-post?

- Roin (2014): the patent system both prevents government from reneging on payouts after an invention appears, and leads to higher rewards to inventors whose inventions turn out to be more valuable

Patents help overcome asymmetric information between inventors and planners, and commitment problems on the part of the government

Ex-post rewards

Ex-post, it may be possible to reduce the deadweight loss of monopoly pricing by patent holders

Kremer (1998) proposes a "patent buyout" where patents are sometimes forced into a public auction and the planner sometimes pays a premium on the auction price in exchange for bringing the invention into the public domain

- Probabilistic aspects ensure that rival firms with information about the value of the invention have an incentive to bid
- Thus, the buyout price does not suffer from a government commitment problem where its incentive to pay falls once invention exists

More on ex-post rewards and buyouts: Shavell and van Ypersele (2001), Khan (2015), and Galasso (2020)

Inefficiencies in direction of research

- Nelson (1959): Firms will perform too little basic research.
  - Uses of basic research are broad, thus unlikely to have value to a firm
  - Basic research is hard to embody in a product, thus hard to patent and license
- Dasgupta and Maskin (1987): The existence of wastefully similar inventions between two firms implies that research portfolios are often too similar.
- Acemoglu (2012): Inventions whose value comes predominantly from follow-on innovations are underprovided
- Bryan and Lemus (2017): Distortions in direction of research are not wholly fixed with policies like patents and research subsidies
- Hopenhayn and Squintani (2021): "Hot" technologies attract too many inventors since none weigh the costs of rivals having to redirect research after a successful invention

Patents smooth market for technology

Inventors differ in their capacity to successfully commercialize an invention [Arora et al. 2001, Teece 1986]

Joint profits are often higher following licensing, since the incumbent and the innovator can act as a monopoly [Gilbert and Newbery 1982]

- Firms may be reluctant to disclose their technology to potential partners and licensors if they think the technology will be expropriated
- Patents limit this risk, by providing legal remedy

However, the possibility of licensing could also distort incentives on margins which affect bargaining over licenses (see, for example, Gans and Stern (2000) on superfluous research)

Secrecy

Firms face a choice between receiving protection for a limited time or relying on secrecy with weaker protection but potentially more time

- Anton and Yao (2004) finds that patents are worth it for minor inventions, but perhaps not for major ones
    - Not getting a patent could signal confidence in a large technological lead, deterring competition
- Scotchmer and Green (1990) notes that secrecy is useful to dynamic invention as well
    - A firm that patents every minor step gives rivals information to create similar inventions that are not covered by the initial patent
- Henry and Ponce (2011) shows that the ability to disclose, in addition to the ability to keep secrets, is useful for appropriating rents.

Avoiding secrecy

For new technologies: incentivizing the development of complements or micro-improvements may be more important for profit than expropriating rents from licensing the underdeveloped technology

- For example, Allen (1983) documents iron producers in 19th century England improving the blast furnace in the absence of patenting
  - Slowing down collective industry improvement with patenting may have led to lower profit
  - Growth in "size of the pie" results in more profit for individual firms
- Nuvolari and Sumner (2013) finds a similar process of collective innovation in the case of porter beer.
- Bessen and Maskin (2009) theorizes that firms may actually be strictly better off if all firms are unable to patent their improvements

Enforcement of IPR

Who should enforce intellectual property rules?

- Should countries enforce patents from abroad?
  - Prior to 1883 Paris Convention, patents were largely unenforced outside of their initial jurisdiction as countries tried to reach the global frontier of innovation [Moser et al. 2011]
- Should poor countries enforce patents at all?
  - Deardorff (1992): Expanding patent protection globally isn't likely to increase welfare due to monopoly pricing
  - Diwan and Rodrik (1991) counters: Lack of IP rights in developing countries will distort inventor effort away from technologies that benefit those countries

Summing up

Patent theory:

- Pros: patents reward inventors for socially valuable ideas and force disclosure to encourage follow-on innovation
- Cons: patent holders can charge above marginal cost, patents can limit diffusion of ideas, and they can distort the direction of innovation

Patent empirics:

- Identifying causal links between patents and innovation remains challenging, though new methods are developing
- Existing literature shows mixed evidence on the effect of patents on innovation
  - Patents seem important in pharmaceuticals and agriculture, but lack positive impact elsewhere and potentially stunt follow-on innovation